8272283 94338344 PMID: 8060309

Membrane bound **CETP** mediates the transfer of free cholesterol between lipoproteins and membranes.

Ruiz-Noriega M; Silva-Cardenas I; Delgado-Coello B; Zentella-Dehesa A; Mas-Oliva J

Instituto de Fisiologia Celular, UNAM, Mexico.

Biochemical and biophysical research communications (UNITED STATES) Aug 15 **1994**, 202 (3) p1322-8, ISSN 0006-291X Journal Code: 0372516

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Cholesteryl ester transfer protein (**CETP**) has been shown to transfer cholesteryl esters among plasma lipoproteins. However, when reconstituted into phosphatidylcholine liposomes, the 74,000 protein mediates above non-specific values the transfer of HDL bound [3H]cholesterol into the artificial membrane system. Employing the known **cDNA sequence** of **CETP** , we synthesized a series of oligonucleotides with specific sequences for different regions of **CETP** and RNA isolated from tissues known to be producers of **CETP** (liver), and tissues not design to synthesize and secrete **CETP** (ovary, lung, intestine and heart). Hybridization experiments showed that independently of the type of tissue tested **CETP** sequences were found. It is suggested that a membrane form of **CETP** might have important repercussions locally.

Membrane bound **CETP** mediates the transfer of free cholesterol between lipoproteins and membranes.

Aug 15 **1994**,

Cholesteryl ester transfer protein (**CETP**) has been shown to transfer cholesteryl esters among plasma lipoproteins. However, when reconstituted into phosphatidylcholine...

30/3,K,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06199990 89215620 PMID: 3244015

Cloning and mRNA tissue distribution of **rabbit** cholesteryl ester transfer protein.

Nagashima M; McLean J W; Lawn R M

Department of Cardiovascular Research, Genentech, Inc., South San Francisco, CA 94080.

Journal of lipid research (UNITED STATES) Dec **1988**, 29 (12) p1643-9, ISSN 0022-2275 Journal Code: 0376606

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The amino acid **sequence** of **rabbit** cholesteryl ester transfer protein (**CETP**) has been obtained from cloned **cDNA** and genomic **sequences**. The 496 amino acid **rabbit CETP** has an overall **sequence** homology of 81% compared to the 476 amino acid human **CETP** , with two-thirds of the amino acid substitutions being conservative. Like human **CETP**, **rabbit CETP** is extremely hydrophobic, which is consistent with its function in the transfer of neutral lipids. The data implies extensive structural similarity between **rabbit** and human **CETP**. **Rabbit CETP** mRNA is estimated to be 2.2 kilobases in size, 300 nucleotides longer than the corresponding human mRNA, and contains the unusual polyadenylation signal **sequence** AGTAAA. In **rabbit**, **CETP** mRNA is found mainly in the liver, with small amounts also present in adrenal glands and kidney. In contrast to human spleen, **rabbit** spleen does not have detectable amounts of **CETP** mRNA. Northern blot analysis of liver poly(A)+ RNAs revealed significant amounts of **CETP** message in human, rhesus, and **rabbit** , and undetectable levels in pig, mouse, and rat, in agreement with reported plasma levels of transfer activity.

```
? ds

Set     Items   Description
S1          0   TETANUS(5N)TOXOID(5N)CDNA
S2      14825   TETANUS(5N)(TOXIN OR TOXOID)
S3     347525   CDNA
S4         96   S2 AND S3
S5         63   S4 AND PY<1996
S6         50   RD (unique items)
S7        129   TETANUS (5N) (CDNA OR GENE)
S8         80   RD (unique items)
S9         33   S8 AND PY<1996
S10   1839226   SEQUENC?
S11        24   S9 AND S10
S12      2872   CMV(5N)PROMOTER
S13    157100   PLASMID
S14       685   S12 AND S13
S15        52   S14 AND PY<1996
S16        23   RD (unique items)
? s rabbit(5n) CETP
          377444  RABBIT
            2579  CETP
     S17      73  RABBIT(5N) CETP
? s cdna or gene
<------User Break------>
u!
? s cetp
     S18    2579  CETP
? s rabbit??
     S19  593032  RABBIT??
? s s18 and s19
            2579  S18
          593032  S19
     S20     246  S18 AND S19
? s (cdna or gene) (5n)sequence
          347525  CDNA
         2197573  GENE
         1521657  SEQUENCE
     S21  225755  (CDNA OR GENE) (5N)SEQUENCE
? s s20 and s21
             246  S20
          225755  S21
     S22      13  S20 AND S21
? rd
>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
     S23      10  RD (unique items)
? s s23 and py<1996
Processing
              10  S23
        27414523  PY<1996
     S24       5  S23 AND PY<1996
? t s24/3,k,ab/1-5

 24/3,K,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

08272283   94338344   PMID: 8060309
   Membrane bound CETP mediates the transfer of free cholesterol
between lipoproteins and membranes.
  Ruiz-Noriega M; Silva-Cardenas I; Delgado-Coello B; Zentella-Dehesa A;
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Mas-Oliva J
Instituto de Fisiologia Celular, UNAM, Mexico.
Biochemical and biophysical research communications (UNITED STATES) Aug 15 **1994**, 202 (3) p1322-8, ISSN 0006-291X Journal Code: 0372516
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Cholesteryl ester transfer protein (**CETP**) has been shown to transfer cholesteryl esters among plasma lipoproteins. However, when reconstituted into phosphatidylcholine liposomes, the 74,000 protein mediates above non-specific values the transfer of HDL bound [3H]cholesterol into the artificial membrane system. Employing the known **cDNA sequence** of **CETP** , we synthesized a series of oligonucleotides with specific sequences for different regions of **CETP** and RNA isolated from tissues known to be producers of **CETP** (liver), and tissues not design to synthesize and secrete **CETP** (ovary, lung, intestine and heart). Hybridization experiments showed that independently of the type of tissue tested **CETP** sequences were found. It is suggested that a membrane form of **CETP** might have important repercussions locally.

Membrane bound **CETP** mediates the transfer of free cholesterol between lipoproteins and membranes.
Aug 15 **1994**,
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...; Sequence; Biological Transport; Carrier Proteins--genetics--GE; Molecular Sequence Data; Oligodeoxyribonucleotides; RNA, Messenger --metabolism--ME; **Rabbits**; Tissue Distribution

24/3,K,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06913966 91154277 PMID: 1999438
Mammalian adipose tissue and muscle are major sources of lipid transfer protein mRNA.
Jiang X C; Moulin P; Quinet E; Goldberg I J; Yacoub L K; Agellon L B; Compton D; Schnitzer-Polokoff R; Tall A R
Department of Medicine, Columbia University, New York, New York 10032.
Journal of biological chemistry (UNITED STATES) Mar 5 **1991**, 266 (7) p4631-9, ISSN 0021-9258 Journal Code: 2985121R
Contract/Grant No.: HL 21006; HL; NHLBI; HL 43165; HL; NHLBI; HL22682; HL ; NHLBI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The plasma cholesteryl ester transfer protein (**CETP**) catalyzes the transfer of cholesteryl esters from high density lipoproteins (HDL) to triglyceride-rich lipoproteins and plays a major role in the catabolism of

HDL. Lipoprotein lipase (LPL) is the rate-limiting enzyme for hydrolysis of circulating triglyceride and is involved in HDL formation. We show that tissues containing LPL are major sources of **CETP** mRNA in several mammalian species, including some with low cholesteryl ester transfer activity in plasma. In hamsters, adipose tissue and heart were found to be the richest sources of both **CETP** and LPL mRNA; in situ hybridization studies showed that the same cell types (i.e. adipocytes or myocytes) contained **CETP** and LPL mRNA in these tissues. Isolated adipocytes synthesized active **CETP**. Dietary studies revealed a complex pattern of response of **CETP** mRNA levels in different tissues, which showed partial similarity to the changes in LPL mRNA abundance. However, high cholesterol diets resulted in increased **CETP** mRNA abundance in adipose tissue, heart, and skeletal muscle, without equivalent changes in LPL mRNA. Plasma HDL cholesteryl ester levels showed strong inverse correlations with **CETP** mRNA abundance in adipose tissue. The results suggest a conserved function of **CETP** in adipose tissue and heart, such as a co-ordinate action with LPL to enhance HDL turnover. Although there is considerable overlap in the tissue- and cell-specific pattern of **CETP** and LPL gene expression, dietary studies revealed only limited parallelism in response at the mRNA level. The increase in **CETP** mRNA in peripheral tissues in response to increased dietary cholesterol suggests that local induction of **CETP** synthesis may help to recycle cholesterol deposited in these tissues during lipolysis of dietary lipoproteins.

Mar 5 **1991**,

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; Amino Acid Sequence; Base **Sequence**; Blotting, Southern; Cloning, Molecular; Diet; **Gene** Expression; Hamsters; Lipoprotein Lipase --genetics--GE; Molecular Sequence Data; Nucleic Acid Hybridization; RNA, Messenger--genetics--GE; **Rabbits**; Rats; Tissue Distribution

Gene Symbol: **CETP**

24/3,K,AB/3 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01925091 Genuine Article#: JM223 Number of References: 20

Title: IDENTIFICATION OF A SEQUENCE WITHIN THE C-TERMINAL-26 AMINO-ACIDS OF CHOLESTERYL ESTER TRANSFER PROTEIN RESPONSIBLE FOR BINDING A NEUTRALIZING MONOCLONAL-ANTIBODY AND NECESSARY FOR NEUTRAL LIPID TRANSFER ACTIVITY (Abstract Available)
Author(s): WANG S; DENG LP; MILNE RW; TALL AR
Corporate Source: COLUMBIA UNIV COLL PHYS & SURG,DEPT MED,DIV MOLEC MED,630 W 168TH ST/NEW YORK//NY/10032; COLUMBIA UNIV COLL PHYS & SURG,DEPT MED,DIV MOLEC MED,630 W 168TH ST/NEW YORK//NY/10032; CLIN RES INST MONTREAL/MONTREAL H2W 1R7/QUEBEC/CANADA/
Journal: JOURNAL OF BIOLOGICAL CHEMISTRY, **1992**, V267, N25 (SEP 5), P 17487-17490
ISSN: 0021-9258
Language: ENGLISH Document Type: NOTE
Abstract: The cholesteryl ester transfer protein (**CETP**; 476 amino acids) mediates the transfer of neutral lipids and phospholipids between plasma lipoproteins. Previous studies showed that the epitope of a neutralizing monoclonal antibody (TP2) was located within the C-terminal 26 amino acids (aa) of **CETP**. To determine possible involvement of this region in lipid transfer activities, we generated six deletion mutants between Arg-451 and Leu-475 by in vitro mutagenesis and expressed mutant proteins in mammalian cells. Only deletion mutants between aa Phe-463 and Leu-475 failed to bind TP2; these mutant proteins were well secreted by cells but showed markedly reduced cholesteryl ester transfer activity. One of the deletion mutants (DELTA-470-475) showed similar reductions in cholesteryl ester and triglyceride transfer activities but normal or increased phospholipid transfer activity. Limited proteolysis of this mutant protein indicated a similar overall folding pattern to the wild-type protein. Thus, aa between Phe-463 and Leu-475 are necessary for binding TP2. Deletions within this sequence selectively impair neutral lipid transfer activity, suggesting a direct involvement in neutral lipid transfer.

, **1992**
Abstract: The cholesteryl ester transfer protein (**CETP**; 476 amino acids) mediates the transfer of neutral lipids and phospholipids between plasma lipoproteins. Previous...

...neutralizing monoclonal antibody (TP2) was located within the C-terminal 26 amino acids (aa) of **CETP**. To determine possible involvement of this region in lipid transfer activities, we generated six deletion...
Research Fronts: 90-0949 001 (RAT GENE ENCODING CHOLESTEROL 7-ALPHA-HYDROXYLASE; EXPRESSION SYSTEM; **RABBIT** SKELETAL-MUSCLE MYOSIN LIGHT CHAIN KINASE; COS CELLS; LH RECEPTORS)
90-2362 001 (STA58 MAJOR...

...SHOCK PROTEIN HSP70 FAMILY)
90-8308 001 (AUTOPHOSPHORYLATED VIRA PROTEIN; SITE-DIRECTED MUTAGENESIS; VARIANT BINDING **SEQUENCE**; ESCHERICHIA-COLI K-12 **GENE** AROG)

24/3,K,AB/4 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01378673 Genuine Article#: GU471 Number of References: 35
Title: THE REGULATION OF HEPATIC LIPASE AND CHOLESTERYL ESTER TRANSFER PROTEIN-ACTIVITY IN THE CHOLESTEROL-FED **RABBIT** (Abstract Available)
Author(s): WARREN RJ; EBERT DL; BARTER PJ; MITCHELL A
Corporate Source: BAKER MED RES INST,COMMERCIAL RD/PRAHRAN/VIC 3181/AUSTRALIA/; UNIV WOLLONGONG/WOLLONGONG/NSW 2500/AUSTRALIA/
Journal: BIOCHIMICA ET BIOPHYSICA ACTA, **1991**, V1086, N3, P354-358

Language: ENGLISH Document Type: ARTICLE
Abstract: Hepatic lipase (HL) and cholesteryl ester transfer protein (**CETP**) activities are both increased in the **rabbit** by cholesterol feeding. The in vivo regulation of HL and **CETP** were explored by examining changes in specific steady-state mRNA levels upon cholesterol feeding. On feeding **rabbits** cholesterol, HL activity increased 3-fold after 2 days and remained at 2.6-times the control value at 28 days. Specific **rabbit** HL mRNA levels were assessed by dot blot analysis of liver poly (A) + RNA hybridized with the human HL cDNA. No significant changes in liver HL mRNA accompanied the increase in activity seen at days 2 and 7. At day 28 a modest rise of 46% was observed. A significant rise in **CETP** activity, evident 7 days after the commencement of cholesterol feeding, was maintained until day 28 when it was 2.4-times the control value. Using the human **CETP** cDNA as probe, **rabbit** liver **CETP** mRNA was also found to increase by day 7, rising to 3.7-times control by day 28. The strong temporal relationship between the rise in **CETP** activity and mRNA ($r = 0.55$, $P = 0.02$) suggests that the regulation of **CETP** may be primarily effected by the levels of specific mRNA. In contrast, the discordance between levels of lipase activity and mRNA suggests that post-transcriptional events may be more important in the regulation of HL in the cholesterol fed **rabbit**.

Title: THE REGULATION OF HEPATIC LIPASE AND CHOLESTERYL ESTER TRANSFER PROTEIN-ACTIVITY IN THE CHOLESTEROL-FED **RABBIT**
, **1991**
Abstract: Hepatic lipase (HL) and cholesteryl ester transfer protein (**CETP**) activities are both increased in the **rabbit** by cholesterol feeding. The in vivo regulation of HL and **CETP** were explored by examining changes in specific steady-state mRNA levels upon cholesterol feeding. On feeding **rabbits** cholesterol, HL activity increased 3-fold after 2 days and remained at 2.6-times the control value at 28 days. Specific **rabbit** HL mRNA levels were assessed by dot blot analysis of liver poly (A) + RNA hybridized...
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...transcriptional events may be more important in the regulation of HL in the cholesterol fed **rabbit**.
Research Fronts: 89-1447 001 (DEVELOPMENTALLY REGULATED **GENE**; CAPPING PROTEIN; **CDNA SEQUENCE**; GENOME ORGANIZATION)

24/3,K,AB/5 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01337586 Genuine Article#: GQ630 Number of References: 46
Title: MOLECULAR-CLONING, SEQUENCE, AND EXPRESSION OF CYNOMOLGUS MONKEY CHOLESTERYL ESTER TRANSFER PROTEIN - INVERSE CORRELATION BETWEEN HEPATIC CHOLESTERYL ESTER TRANSFER PROTEIN MESSENGER-RNA LEVELS AND PLASMA HIGH-DENSITY-LIPOPROTEIN LEVELS (Abstract Available)
Author(s): PAPE ME; REHBERG EF; MAROTTI KR; MELCHIOR GW
Corporate Source: UPJOHN CO,METAB DIS RES,7250-209-4/KALAMAZOO//MI/49001; UPJOHN CO,MOLEC BIOL RES/KALAMAZOO//MI/49001
Journal: ARTERIOSCLEROSIS AND THROMBOSIS, **1991**, V11, N6, P1759-1771
Language: ENGLISH Document Type: ARTICLE

Abstract: A cDNA clone containing the coding region for cynomolgus monkey cholesteryl ester transfer protein (**CETP**) was isolated by the polymerase chain reaction with primers based on the human **CETP cDNA sequence** and **cDNA** synthesized from liver poly (A+) RNA. Analysis of that cDNA indicated that the nucleotide and amino acid sequences of cynomolgus monkey **CETP** were greater than 95% homologous with the human sequences. A fragment of the cDNA was used to develop an internal-standard/RNAse protection assay that allowed precise quantification of **CETP** mRNA levels. Analysis of total RNA from various tissues with this assay revealed that the liver and thoracic aorta expressed high levels of **CETP** mRNA; the mesenteric fat, adrenal gland, spleen, and abdominal aorta had low but detectable levels of the mRNA; and the brain, kidney, intestine, and skeletal muscle had undetectable levels of that mRNA. When the monkeys were made hypercholesterolemic by a high-fat, high-cholesterol (HFHC) diet, hepatic levels of **CETP** mRNA increased from 1.6 +/- 0.4 pg/mu-g total RNA (mean +/- SEM) to 4.1 +/- 0.8 pg/mu-g ($p < 0.005$); mesenteric fat **CETP** mRNA increased from 0.4 +/- 0.1 pg/mu-g total RNA to 5.3 +/- 2.2 pg/mu-g ($p < 0.05$); and plasma CET activity increased approximately fourfold. The **CETP** mRNA levels in the thoracic and abdominal aortas were not significantly increased in monkeys fed the HFHC diet, even though those animals had gross atherosclerosis. The apoprotein E mRNA levels, however, were markedly increased in the aortas of monkeys with atherosclerosis, with the largest increase occurring in the abdominal aorta. Taken together, these data suggest that lipid deposition in the artery was not accompanied by increased expression of the CEPT gene in that tissue. Statistical analysis showed that a strong, negative correlation existed between hepatic **CETP** mRNA levels and both high density lipoprotein cholesterol ($r = -0.85$, $p < 0.001$) and apoprotein A-I ($r = -0.84$, $p < 0.001$). These data suggest that HFHC diet-induced changes in high density lipoprotein metabolism may be linked to altered expression of a functional **CETP** gene.

, **1991**

Abstract: A cDNA clone containing the coding region for cynomolgus monkey cholesteryl ester transfer protein (**CETP**) was isolated by the polymerase chain reaction with primers based on the human **CETP cDNA sequence** and **cDNA** synthesized from liver poly (A+) RNA. Analysis of that cDNA indicated that the nucleotide and amino acid sequences of cynomolgus monkey **CETP** were greater than 95% homologous with the human sequences. A fragment of the cDNA was used to develop an internal-standard/RNAse protection assay that allowed precise quantification of **CETP** mRNA levels. Analysis of total RNA from various tissues with this assay revealed that the liver and thoracic aorta expressed high levels of **CETP** mRNA; the mesenteric fat, adrenal gland, spleen, and abdominal aorta had low but detectable levels...

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...changes in high density lipoprotein metabolism may be linked to altered expression of a functional **CETP** gene.

...Identifiers--LIPID TRANSFER PROTEINS; A-I METABOLISM; ATHEROGENIC DIET;
APOLIPOPROTEIN-E; **RABBIT**; ATHEROSCLEROSIS; TISSUE; LIVER; DOGS;
DNA
Research Fronts: 89-1447 002 (DEVELOPMENTALLY REGULATED **GENE**;
CAPPING PROTEIN; **CDNA SEQUENCE**; GENOME ORGANIZATION)
89-2539 001 (LOW-DENSITY LIPOPROTEIN METABOLISM; LDL RECEPTOR; RAT
AORTIC SMOOTH-MUSCLE...
?

08345226 95033197 PMID: 7946324

An efficient expression, purification and immunodetection system for recombinant gene products.

Baier G; Baier-Bitterlich G; Couture C; Telford D; Giampa L; Altman A
La Jolla Institute for Allergy and Immunology, CA.

BioTechniques (UNITED STATES) Jul **1994**, 17 (1) p94, 96, 98-9,
ISSN 0736-6205 Journal Code: 8306785
Contract/Grant No.: CA35299; CA; NCI
Document type: Technical Report
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

We describe a modification of the mammalian expression vector pRc/CMV, which drives expression of inserted genes from either the human cytomegalovirus (**CMV**) immediate-early **promoter** or the bacteriophage T7 RNA polymerase promoter. The modification is designed to allow expression, simple purification and specific immunodetection of recombinant fusion proteins. The modified **plasmid** , termed pTag/CMV-neo, encodes a Kozak consensus ribosome-binding site (RBS) and a 30-amino acid fusion tag peptide. This peptide consists of a metal ion-binding site, (His)6, for single-step affinity purification using Ni(2+)-chelating resin and a multi-purpose HIV-1-derived peptide (p18HIV). This viral epitope can be used to identify, detect and characterize target fusion proteins in conjunction with a specific monoclonal antibody H902 that does not display cross-reactivity with cellular proteins. The H902 production hybridoma cell line is reagent #521 from the NIH AIDS Research and Reference Program.

Jul **1994**,
... expression vector pRc/CMV, which drives e

299221 94365494 PMID: 8083602

The HIV-1 regulatory protein Nef has a specific function in viral expression in a murine macrophage cell line.

Murphy K M; Sweet M J; Hume D A

Centre for Molecular Biology and Biotechnology, University of Queensland, Australia.

Journal of leukocyte biology (UNITED STATES) Sep **1994**, 56 (3) p294-303, ISSN 0741-5400 Journal Code: 8405628

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Expression of reporter genes under the control of the HIV-1 long terminal repeat (LTR) was up-regulated in the murine macrophage cell line RAW264 by cotransfection of a **plasmid** coding for the viral regulatory protein Nef. To determine if a discrete section of the LTR was exclusively responsive to Nef, a series of promoters was produced by successive 5' deletions from the LTR up to the boundary of the enhancer region. These truncated promoters were as active as the full-length sequence in the RAW264 cells, but elimination of the direct repeats and one of the three Sp1 sites reduced promoter activity to minimal levels. Transcription driven by all constructs was equally susceptible to the trans-activating effect of Nef and could be increased further by the addition of a Tat-expressing **plasmid** to the cotransfection. Open reading frames of nef from NL4-3, from HXB2, which has a premature stop, and a fully functional hybrid of the two under the control of the SR alpha artificial promoter (SV40 early promoter plus HTLV-I R-U5') were able to transactivate the LTR in RAW264 cells to the same degree as HXB3 nef under the control of the cytomegalovirus (**CMV**) immediate-early **promoter**. A frameshift mutation of Nef at the XhoI site at position 8475 did not abrogate trans-activation of the LTR in macrophages. To further define the effective trans-activation region of Nef, internal deletions were made. Changes downstream of the XhoI site at amino acid 35 resulted in little or no reduction in trans-activation, whereas a deletion between the **CMV promoter** of the expression **plasmid** and the XhoI site largely abolished activity. Nef trans-activation of the LTR may be restricted to macrophages. Parallel cotransfection experiments in COS-1 simian fibroblast-like cells showed repression of reporter expression by Nef. Results suggested that the section of nef responsible for transactivation of the LTR in macrophages differed slightly from that sufficient for trans-repression in fibroblasts. Translation of the protein from the first translation start site (Met-1) rather than from the second in-frame ATG (Met-20) appears to be necessary for the trans-activating effect of Nef in RAW264 cells. Mutation of the initial ATG to ATA led to loss of trans-activating activity. Expression of Nef also has a cytostatic/cytotoxic effect on RAW264 cells indicated by a reduced rate of establishment of stably transfected clones. The cytostatic effect of Nef was not relieved by internal deletions in the coding sequence. (ABSTRACT TRUNCATED AT 400 WORDS)

Sep **1994**,

... LTR) was up-regulated in the murine macrophage cell line RAW264 by cotransfection of a **plasmid** coding for the viral regulatory protein Nef. To determine if a discrete section of the...

... effect of Nef and could be increased further by the addition of a Tat-expressing **plasmid** to the cotransfection. Open reading frames of nef from NL4-3, from HXB2, which has...

... RAW264 cells to the same degree as HXB3 nef under the control of the cytomegalovirus (**CMV**) immediate-early **promoter**. A frameshift mutation of Nef at the XhoI site at position 8475 did not abrogate...

... 35 resulted in little or no reduction in trans-activation, whereas a

deletion between the **CMV promoter** of the expression **plasmid** and the XhoI site largely abolished activity. Nef trans-activation of the LTR may be...

16/3,K,AB/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05375476 87053814 PMID: 3536478

Tetanus toxin: primary structure, expression in E. coli, and homology with botulinum toxins.

Eisel U; Jarausch W; Goretzki K; Henschen A; Engels J; Weller U; Hudel M; Habermann E; Niemann H

EMBO journal (ENGLAND) Oct **1986**, 5 (10) p2495-502, ISSN 0261-4189 Journal Code: 8208664

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

A pool of synthetic oligonucleotides was used to identify the **gene** encoding **tetanus** toxin on a 75-kbp plasmid from a toxigenic non-sporulating strain of Clostridium tetani. The nucleotide **sequence** contained a single open reading frame coding for 1315 amino acids corresponding to a polypeptide with a mol. wt of 150,700. In the mature toxin molecule, proline (2) and serine (458) formed the N termini of the 52,288 mol. wt light chain and the 98,300 mol. wt heavy chain, respectively. Cysteine (467) was involved in the disulfide linkage between the two subchains. The amino acid **sequences** of the tetanus toxin revealed striking homologies with the partial amino acid **sequences** of botulinum toxins A, B, and E, indicating that the neurotoxins from C. tetani and C. botulinum are derived from a common ancestral gene. Overlapping peptides together covering the entire tetanus toxin molecule were synthesized in Escherichia coli and identified by monoclonal antibodies. The promoter of the toxin gene was localized in a region extending 322 bp upstream from the ATG codon and was shown to be functional in E. coli.

Oct **1986**,

11/3,K,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07945496 94011029 PMID: 8406568

Analysis of human T-cell receptor V beta **gene** usage following immunization to **tetanus** toxoid in vivo.

Hibberd M L; Wong F S; Nicholson L B; Demaine A G
Department of Medicine, King's College School of Medicine and Dentistry, London.

Immunology (ENGLAND) Jul **1993**, 79 (3) p398-402, ISSN 0019-2805 Journal Code: 0374672
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The human T-cell antigen receptor (TcR) V beta repertoire was investigated following in vivo reimmunization with tetanus toxoid (TT). Four healthy subjects were immunized subcutaneously with TT, and 24 samples of peripheral blood T cells were taken at intervals over several weeks and used to generate TcR-C beta chain-specific first-strand cDNA. A semi-quantitative assay utilizing the polymerase chain reaction (PCR) was used to measure the amount of 22 different TcR-V beta gene transcripts in the cDNA. A peak increase in the amount of V beta 2, 4, 6, 13.1 and 14 occurred 14 days post-immunization, with each V beta increased in at least two of the four subjects. No obvious changes in the other 17 V beta genes were found. A secondary antibody response to TT occurred in all subjects by day 14. These results show that it is now possible to characterize the in vivo kinetics of the human TcR repertoire following stimulation with a conventional antigen.

```
? ds

Set      Items   Description
S1           0   TETANUS(5N)TOXOID(5N)CDNA
S2       14825   TETANUS(5N)(TOXIN OR TOXOID)
S3      347525   CDNA
S4          96   S2 AND S3
S5          63   S4 AND PY<1996
S6          50   RD (unique items)
S7         129   TETANUS (5N) (CDNA OR GENE)
S8          80   RD (unique items)
S9          33   S8 AND PY<1996
S10    1839226   SEQUENC?
S11         24   S9 AND S10
? s cmv(5n)promoter
           29753  CMV
          304756  PROMOTER
     S12    2872  CMV(5N)PROMOTER
? s plasmid
     S13  157100  PLASMID
? s s12 and s13
            2872  S12
          157100  S13
     S14     685  S12 AND S13
? s s14 and py<1996
Processing
             685  S14
        27414523  PY<1996
     S15      52  S14 AND PY<1996
? rd
>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
...examined 50 records  (50)
...completed examining records
     S16      23  RD (unique items)
```

```
      ---  -----  -----------
? s cmv(5n)promoter
            655  CMV
          16805  PROMOTER
      S1    284  CMV(5N)PROMOTER
? s s1 and py<1997
            284  S1
        2818514  PY<1997
      S2     20  S1 AND PY<1997
? t s2/3,k,ab/1-5

 2/3,K,AB/1
DIALOG(R)File 340:CLAIMS(R)/US Patent
(c) 2003 IFI/CLAIMS(R). All rts. reserv.

Dialog Acc No: 3775852  IFI Acc No: 0239422
Document Type: C
ENDOMETRIAL FUNCTION
Inventors: Charnock-Jones David Stephen (GB); Heap Robert Brian (GB);
    Sharkey Andrew Mark (GB); Smith Stephen Kevin (GB)
Assignee: Cambridge University Technical Services Ltd GB
Assignee Code: 47628
Publication (No,Date), Applic (No,Date):
US 6472374     20021029 US 97860047    19970918
Publication Kind:  B
Calculated Expiration: 20151221
PCT Pub(No,Date),Applic(No,Date): WO 9620013      19960704  WO
95GB3008    19951221
    Section 371:  19970918
    Section 102(e):19970918
Priority Applic(No,Date): GB 9426380     19941224; GB 9520879     19951012

Abstract: Disclosed is a method of altering one or more characteristics of
at least some of the cells of the reproductive tract of a mammalian
individual by the  introduction into said cells of a nucleic acid, together
with a composition  comprising nucleic acid, for use in the method.


...PCT Pub(No,Date),Applic(No,Date): 19960704
Non-exemplary Claims: ...7. The method of claim 1, wherein the
   promoter is the CMV promoter.
...

...9. The method of claim 8, wherein the promoter is the CMV
   promoter.


 2/3,K,AB/2
DIALOG(R)File 340:CLAIMS(R)/US Patent
(c) 2003 IFI/CLAIMS(R). All rts. reserv.

Dialog Acc No: 3707410  IFI Acc No: 0221264
Document Type: C
GENE THERAPY FOR RESTENOSIS USING AN ADENOVIRAL VECTOR; TREATMENT OF
RESTENOSIS BY GENE THERAPY, COMPRISING THE ADMINISTRATION OF A RECOMBINANT
ADENOVIRUS CONTAINING A SUICIDE GENE
Inventors: Branellec Didier (FR); Dedieu Jean-Francois (FR); Denefle
    Patrice (FR); Feldman Laurent (FR); Perricaudet Michel (FR); Steg
    Philippe Gabriel (FR)
Assignee: Aventis Pharma S A FR
Assignee Code: 53500
Publication (No,Date), Applic (No,Date):
US 6410011     20020625 US 96633769    19960620
Publication Kind:  B
```

Calculated Expiration: 20150810
PCT Pub(No,Date),Applic(No,Date): WO 965321 **19960222** WO 95FR1074 19950810
Section 371: 19960620
Section 102(e):19960620
Priority Applic(No,Date): FR 9410083 19940817

Abstract: A method for treating restenosis by gene therapy is disclosed, said method comprising delivering a recombinant suicide-genecontaining adenovirus.

...PCT Pub(No,Date),Applic(No,Date): **19960222**
Non-exemplary Claims: ...wherein the promoter is selected from the group consisting of a RSV LTR and a **CMV promoter**.

2/3,K,AB/3
DIALOG(R)File 340:CLAIMS(R)/US Patent
(c) 2003 IFI/CLAIMS(R). All rts. reserv.

Dialog Acc No: 3678809 IFI Acc No: 0214446
Document Type: C
CELL-SPECIFIC ACTIVE COMPOUNDS REGULATED BY THE CELL CYCLE; DNA CONSTRUCT OF AN ACTIVATOR SEQUENCE, A CELL CYCLE-CONTROLLED PROMOTER, AND DNA WHICH CODES FOR AN ACTIVE SUBSTANCE; GENE THERAPY
Inventors: Muller Rolf (DE); Sedlacek Hans-Harald (DE)
Assignee: Hoechst AG DE
Assignee Code: 29472
Publication (No,Date), Applic (No,Date):
US 6384202 20020507 US 97793109 19970425
Publication Kind: B
Calculated Expiration: 20150825
PCT Pub(No,Date),Applic(No,Date): WO 966941 **19960307** WO 95EP3371 19950825
Section 371: 19970425
Section 102(e):19970425
Priority Applic(No,Date): GB 9417366 19940826; GB 956466 19950329; DE 19524720 19950712

Abstract: A DNA sequence is described for the gene therapy of diseases associated with the immune system. In its essential elements, the DNA sequence is composed of an activator sequence, a promoter module and a gene for the active substance. The activator sequence is activated in a cell-specific or virus-specific manner and this activation is regulated by the promoter module in a cell cycle-specific manner. The choice of activator sequence and active substance depends on the indication area. The DNA sequence is inserted into a viral or non-viral vector which is supplemented by a ligand having affinity for the target cell. Depending on the choice of activator sequence and active substance, the following can be treated by administering the DNA sequence: defective formation of blood cells; autoimmune diseases and allergies and, in addition, rejection reactions against transplanted organs; chronic arthritis; viral and parasitic infections and, in addition, prophylaxis of viral, bacterial and parasitic infections; and leukemias.

...PCT Pub(No,Date),Applic(No,Date): **19960307**
Non-exemplary Claims: ...4. The active compound as claimed in claim 3, containing the **CMV promoter** sequence, the **CMV** enhancer sequence or the SV40 **promoter** sequence...

2/3,K,AB/4

DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 3650798 IFI Acc No: 0206935
Document Type: C
DNA FOR EXPRESSION UNDER CONTROL OF A CELL CYCLE-DEPENDENT PROMOTER; NUCLEOTIDE SEQUENCES PREFERENTIAL POLYPEPTIDES FOR USE IN THE TREATMENT OF DEFECTS IN CENTRAL NERVOUS SYSTEM
Inventors: Muller Rolf (DE); Sedlacek Hans-Harald (DE)
Assignee: Aventis Pharma Deutschland GmbH DE
Assignee Code: 52914
Publication (No,Date), Applic (No,Date):
US 6358732 20020319 US 97793110 19970425
Publication Kind: B
Calculated Expiration: 20150825
PCT Pub(No,Date),Applic(No,Date): WO 966939 **19960307** WO 95EP3369 19950825
Section 371: 19970425
Section 102(e):19970425
Priority Applic(No,Date): GB 9417366 19940826; GB 956466 19950329

Abstract: A DNA sequence is disclosed for the genetic therapy of diseases of the central nervous system. The essential components for the DNA sequence are the activator sequence, the promoter module, and the active substance coding gene. The activator sequence is specifically activated in activated endothelial or glial cells. Activation is cell cycle-regulated by the promoter module. The active substance represents an inhibitor of the nerve growth factor, a dopanine metabolism enzyme, and/or a nerve cell protection factor. The disclosed DNA sequence is inserted into a viral or non-viral vector, supplemented with a ligand with affinity for the target cells.

...PCT Pub(No,Date),Applic(No,Date): **19960307**
Non-exemplary Claims: ...of claim 1, wherein said activator sequence is selected from the group consisting of: a **CMV promoter**, a **CMV** enhancer and a SV40 **promoter**.

2/3,K,AB/5
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 3600051 IFI Acc No: 0141864
Document Type: C
VIABLE CONTAMINANT PARTICLE FREE ADENOVIRUSES, THEIR PREPARTION AND USE; GENETICALLY ENGINEERED REPLICATION DEFECTIVE VIRAL VECTOR FOR USE AS A TOOL IN GENE THERAPY
Inventors: Orsini Cecile (FR); Perricaudet Michel (FR); Yeh Patrice (FR)
Assignee: Rhone-Poulenc Rorer S A FR
Assignee Code: 27977
Publication (No,Date), Applic (No,Date):
US 6312946 20011106 US 97817575 19970422
Publication Kind: B
Calculated Expiration: 20151025
PCT Pub(No,Date),Applic(No,Date): WO 9613596 **19960509** WO 95FR1415 19951025
Section 371: 19970422
Section 102(e):19970422
Priority Applic(No,Date): FR 9413355 19941028

Abstract: Novel adenovirus-derived viral vectors, the preparation thereof, and their use in gene therapy, are disclosed. In particular, recombinant adenoviruses including an adenovirus genome wherein (i) the E1 region is

inactivated, (ii) the genomic organization is modified, and (iii) optional recombination with the producing line genome generates non-viable viral particles, are disclosed.

...PCT Pub(No,Date),Applic(No,Date): **19960509**
Non-exemplary Claims: ...the viral promoter is selected from the group consisting of an E1A, an MLP, a **CMV**, and an RSV **promoter**.
?

```
 s rabbit(5n) CETP
            1066  RABBIT
              89  CETP
      S3       3  RABBIT(5N) CETP
? rd
>>>Duplicate detection is not supported for File 340.
>>>All specified files are unsupported, command ignored.
? t s3/3,k,ab/1-3

 3/3,K,AB/1
DIALOG(R)File 340:CLAIMS(R)/US Patent
(c) 2003 IFI/CLAIMS(R). All rts. reserv.

Dialog Acc No: 10356103  IFI Acc No: 2003-0100520  IFI Acc No: 2003-0028341
Document Type: C
IMMUNOLOGICAL PROCESS AND CONSTRUCTS FOR INCREASING THE HDL CHOLESTEROL
CONCENTRATION BY DNA VACCINATION
Inventors: GLENN KEVIN (US); NEEDLEMAN PHILIP (US)
Assignee: Unassigned Or Assigned To Individual
Assignee Code: 68000
Publication (No,Date), Applic (No,Date):
US 20030100520 20030529 US 99386591    19990831
Publication Kind:  A1
Continuation Pub(No),Applic(No,Date):                              US 97934367
  19970919
Cont.-in-part Pub(No),Applic(No,Date):                              US
97785997     19970121;                          US 97788882     19970121
Priority Applic(No,Date): US 99386591    19990831; US 97934367    19970919;
US 97785997    19970121; US 97788882    19970121

Abstract: A process for inducing the production of antibodies that bind to
cholesteryl  ester transfer protein (CETP) is disclosed. That process
comprises the steps of: (a) immunizing a mammal with an inoculum containing
a recombinant DNA molecule that comprises a DNA sequence that contains (i)
a sequence encoding a CETP immunogen that is linked to (ii) a promoter
sequence that controls expression of the CETP immunogen, the recombinant
DNA molecule being dissolved or dispersed in a vehicle; and (b) maintaining
the immunized  mammal for a time period sufficient to induce the production
of antibodies that bind to CETP, and preferably lessen the transfer of
cholesteryl esters from HDL where the blood of the mammal itself contains
CETP. Immunogens, inocula, DNA segments, and recombinant DNA molecule
vectors useful for carrying out the invention are also disclosed.


Non-exemplary Claims: ...7. The process according to claim 3 wherein said
   recombinant DNA molecule encodes rabbit CETP as said
   immunogenic polypeptide...


 3/3,K,AB/2
DIALOG(R)File 340:CLAIMS(R)/US Patent
(c) 2003 IFI/CLAIMS(R). All rts. reserv.

Dialog Acc No: 10277401  IFI Acc No: 2003-0021804  IFI Acc No: 2003-0005236
Document Type: C
IMMUNOLOGICAL PROCESS FOR INCREASING THE HDL CHOLESTROL CONCENTRATION
Inventors: GLENN KEVIN (US); NEEDLEMAN PHILIP (US)
Assignee: Unassigned Or Assigned To Individual
Assignee Code: 68000
Publication (No,Date), Applic (No,Date):
US 20030021804 20030130 US 97785997    19970121
Publication Kind:  A1
Priority Applic(No,Date): US 97785997    19970121
```

Abstract: A process for increasing the concentration of HDL cholesterol in the blood of a mammal whose blood contains cholesterol ester transfer protein (CETP) is contemplated. That process comprises the steps of: (a) immunizing the mammal with an inoculum containing a CETP immunogen that is an immunogenic polypeptide having a CETP amino acid residue sequence and is dissolved or dispersed in a vehicle; and (b) maintaining the immunized mammal for a time period sufficient for said immunogenic polypeptide to induce the production of antibodies that bind to CETP and lessen the transfer of cholesteryl esters from HDL. Immunogens, inocula and DNA segments useful for carrying out the invention are also disclosed.

Non-exemplary Claims: ...according to claim 1 wherein said immunogenic polypeptide has the amino acid residue sequence of **rabbit CETP**.

3/3,K,AB/3
DIALOG(R)File 340:CLAIMS(R)/US Patent

Dialog Acc No: 3707419 IFI Acc No: 0221273
Document Type: C
MONOCLONAL ANTIBODY REACTIVE TO HUMAN CETP AND ASSAY METHOD FOR HUMAN CETP; ANTI-HUMAN CHOLESTERYL ESTER TRANSFER PROTEIN MONOCLONAL ANTIBODY OR FAB FRAGMENT WHICH INHIBITS CHOLESTEROL ESTER TRANSFER ACTIVITY OF HUMAN CETP AND DOES NOT INHIBIT ACTIVITY OF **RABBIT CETP**
Inventors: Kamada Masafumi (JP); Okamoto Hiroshi (JP); Tamatani Takuya (JP)
Assignee: Japan Tobacco Inc JP
Assignee Code: 43797
Publication (No,Date), Applic (No,Date):
US 6410020 20020625 US 2000615404 20000712
Publication Kind: B
Calculated Expiration: 20200712
Priority Applic(No,Date): JP 95134836 19950502

Abstract: Monoclonal antibodies which have binding specificity to human CETP(CETP inhibition activity) and which are useful as reagents for purification or quantification of human CETP, and as pharmaceuticals to prevent and/or treat hyperlipidemia or arteriosclerosis are provided. Furthermore, purification and quantification methods of human CETP by using the monoclonal antibodies are also provided.

...WHICH INHIBITS CHOLESTEROL ESTER TRANSFER ACTIVITY OF HUMAN CETP AND DOES NOT INHIBIT ACTIVITY OF **RABBIT CETP**

Exemplary Claim: ...ester transfer activity of human CETP and does not inhibit cholesterol ester transfer activity of **rabbit CETP** at a concentration of 3 mu g/ml or below, and wherein said monoclonal antibody...
?

4/3,K,AB/5 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03950134 Genuine Article#: QU741 Number of References: 33
Title: FUSIONAL EXPRESSION OF HUMAN **CHOLESTERYL ESTER TRANSFER PROTEIN** CDNA IN RECOMBINANT VACCINIA VIRUS-INFECTED MAMMALIAN-CELLS
Author(s): YOON WH; JANG MK; BOK SH; PARK KB
Corporate Source: KYUNGPOOK NATL UNIV,COLL NAT SCI,DEPT GENET ENGN/TAEGU 702701//SOUTH KOREA/; KYUNGPOOK NATL UNIV,COLL NAT SCI,DEPT GENET ENGN/TAEGU 702701//SOUTH KOREA/; KOREA RES INST BIOSCI & BIOTECHNOL,BIOPROD RES GRP/TAEJON 305606//SOUTH KOREA/
Journal: MOLECULES AND CELLS, 1995, V5, N2 (APR 30), P107-113
ISSN: 1016-8478
Language: ENGLISH Document Type: ARTICLE
Abstract: Biologically active human plasma **cholesteryl ester transfer protein** (**CETP**) was directed to produce as a fusion protein with **glutathione**-S-transferase (**GST**) in recombinant vaccinia virus-infected mammalian cells, Complementary DNAs for CST and **CETP** were Ligated side by side, and introduced into vaccinia viral transfer vectors. The viral vectors were transfected into CV-1 cells infected previously with wild-type vaccinia viruses, Recombinant viruses were generated by the homologous recombination and selected with BUdR and X-gal in human TK- 143B cells. The DNA from the selected virus was amplified and expressed in the CV-1 cells, The **GST/CETP** fusion protein (86 kDa) was identified on the SDS-PAGE followed by Western blot analysis using polyclonal antibody against the C-terminal active region of **CETP** fused with **GST** , The virus-infected cell lysates were loaded on the **glutathione** -Sepharose affinity column and the **CETP** was eluted from the column by cleavage with thrombin while the **GST/CETP** was bound on the column, The purified **CETP** showed biological activity when subjected to a **CETP** assay.

Title: FUSIONAL EXPRESSION OF HUMAN **CHOLESTERYL ESTER TRANSFER PROTEIN** CDNA IN RECOMBINANT VACCINIA VIRUS-INFECTED MAMMALIAN-CELLS

9/3,K,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09033505 96417308

Structure-function relationships of human **cholesteryl ester transfer protein**: analysis using monoclonal **antibodies**.

Roy P; MacKenzie R; Hirama T; Jiang XC; Kussie P; Tall A; Rassart E; Milne R

Departement des Sciences Biologiques, Universite du Quebec a Montreal, Canada.

Journal of lipid research (UNITED STATES) Jan 1996, 37 (1) p22-34, ISSN 0022-2275 Journal Code: IX3

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Cholesteryl ester transfer protein (**CETP**), a 476 amino acid glycoprotein, mediates cholesteryl ester (CE), triglyceride, and phospholipid transfer among plasma lipoproteins. A monoclonal **antibody** (mAb), TP2, specific for an epitope within the last 26 amino acids of **CETP** has been shown to block all **CETP** -mediated lipid transfer, apparently by limiting access to lipid-binding sites in the carboxy terminal of **CETP**. A new panel of 16 anti-human **CETP** mAbs has now been used to further probe the structure-function relationships of **CETP**. Of the new mAbs, 9 partially inhibit **CETP**-mediated CE transfer (24-43%) from HDL to LDL. The corresponding epitopes were mapped within the **CETP** primary structure by the reactivity of the mAbs with **CETP** variants having deletions or amino acid substitutions. Of the 9 new, neutralizing mAbs, 6 are specific for epitopes situated between residues 410-450 and two others for epitopes between residues 184-260 and 332-366, respectively. The epitope of one neutralizing mAbs could not be mapped. Therefore, binding of mAbs to epitopes situated in four non-overlapping regions within **CETP** primary structure that are separated by as many as 280 residues can neutralize **CETP** -mediated CE transfer. Epitopes of mAbs that do not influence CE transfer activity map to the regions 184-260, 261-331, and 367-409, respectively. When pairs of mAbs were tested for their abilities to mutually compete for binding to immobilized **CETP**, competition was observed for mAbs specific for epitopes that are distant in **CETP** primary structure. The cross-competition patterns demonstrate that the carboxy terminal 60% of **CETP** adopts a compact structure. Together with previous mutagenesis studies, the data suggests that a carboxy terminal neutral lipid binding domain may be in close proximity to a lipoprotein binding region within native **CETP**.

Structure-function relationships of human **cholesteryl ester**

Dialog Acc No: 2864290 IFI Acc No: 9719947
Document Type: C
TIGHT CONTROL OF GENE EXPRESSION IN EUCARYOTIC CELLS BY TETRACYCLINE-RESPONSIVE PROMOTERS
Inventors: Bujard Hermann (DE); Gossen Manfred (DE); Salfeld Jochen G (US); Voss Jeffrey W (US)
Assignee: BASF AG DE; Knoll AG DE Assignee Code: 04911 07016
Patent (No,Date), Applic (No,Date)
US 5650298 **19970722** US 94260452 19940614
Calculated Expiration: 20140722
(Cited in 001 later patents)
Cont.-in-part Pat(No),Applic(No,Date): ABANDONED US 9376327 19930614
Priority Applic(No,Date): US 94260452 19940614; US 9376327 19930614

Abstract:
Transgenic animals carrying two transgenes, the first coding for a transactivator fusion protein comprising a tet repressor and a polypeptide which directly or indirectly activates in eucaryotic cells, and the second comprising a gene operably linked to a minimal **promoter** operably linked to at least one tet operator sequence, are disclosed. Isolated DNA molecules (e.g., targeting vectors) for integrating a polynucleotide sequence encoding a transactivator of the invention at a predetermined location within a second target DNA molecule by homologous recombination are also disclosed. Transgenic animals having the DNA molecules of the invention integrated at a predetermined location in a chromosome by homologous recombination are also encompassed by the invention. Methods to regulate the expression of a tet operator linked-gene of interest by administering tetracycline or a tetracycline analogue to an animal of the invention are also disclosed. The regulatory system of the invention allows for conditional inactivation or modulation of expression of a gene of interest in a host cell or animal.

Patent (No,Date), Applic (No,Date)
... **19970722**

Abstract:
...activates in eucaryotic cells, and the second comprising a gene operably linked to a minimal **promoter** operably linked to at least one tet operator sequence, are disclosed. Isolated DNA molecules (e...
Non-exemplary Claims:
...for integrating a polynucleotide sequence encoding a tetracycline-controllable transactivator (tTA) and a tTA-responsive **promoter** within a predetermined gene of interest in a second target DNA molecule, the DNA molecule...

...activates transcription in eucaryotic cells; and c) a third polynucleotide sequence comprising a tTA-responsive **promoter**, operably linked to: d) a fourth polynucleotide sequence comprising at least a portion of a...

...of interest and expression of the gene of interest is controlled by the tTA-responsive **promoter**.
...21. The DNA molecule of claim 11, wherein the tTA-responsive **promoter** of the third nucleotide sequence comprises a minimal **promoter** operably linked to at least one tet operator sequence...

...22. The DNA molecule of claim 21, wherein the minimal **promoter** is

derived from a **cytomegalovirus immediate early** gene **promoter** or a herpes simplex virus thymidine kinase gene **promoter**.

...claim 25, further comprising a gene of interest operably linked to a tTA-responsive transcriptional **promoter**.

...

...27. The host cell of claim 26, wherein the tTA-responsive **promoter** comprises a minimal **promoter** operably linked to at least one tet operator sequence...

...28. The host cell of claim 27, wherein the minimal **promoter** is derived from a **cytomegalovirus immediate early** gene **promoter** or a herpes simplex virus thymidine kinase gene **promoter**.

...

...method for inhibiting transcription of the gene of interest operatively linked to the tTA-responsive **promoter** in the host cell of claim 26, comprising contacting the cell with tetracycline or a...gene product encoded by the gene of interest operably linked to the tTA-responsive transcriptional **promoter** in the cell of claim 26, comprising: a) growing cells in a culture medium in...